

Attorney Docket No.: 6535.200-US
USSN: 10/671,064
Filed: September 25, 2003
Inventor: Christensen et al.
Via Facsimile No.: 571-273-8300

Amendments to the Claims:

The listing of claims will replace all prior versions, and listings, of the claims in the application:

Listing of Claims

Claim 1 (Currently Amended) A process for purifying a fermentation-derived product protein with a molar weight of less than 25000 Dalton, said process comprising microfiltration of a fermentation broth containing the product protein at a microfiltration temperature within the range from 66 °C to 90 °C.

Claim 2 (Previously Presented) The process according to claim 1, wherein said microfiltration is performed in the absence of activated carbon.

Claim 3 (Previously Presented) The process according to claim 1, wherein the microfiltration temperature is within the range from 70 °C to 90 °C.

Claim 4 (Previously Presented) The process according to claim 1, wherein the microfiltration temperature is within the range from 70 °C to 80 °C.

Claim 5 (Previously Presented) The process according to claim 1, wherein the microfiltration is performed as a cross flow microfiltration.

Claim 6 (Previously Presented) The process according to claim 5, wherein the microfiltration process is performed with a vibrating microfiltration membrane.

Claim 7 (Previously Presented) The process according to claim 5, wherein the microfiltration process is performed with backshock.

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Claim 8 (Previously Presented) The process according to claim 1, wherein the microfiltration process is performed using a microfiltration membrane formed from a material selected from the group consisting of natural polymers, synthetic polymers, ceramics, metals and mixtures thereof

Claim 9 (Previously Presented) The process according to claim 1, wherein the microfiltration process is performed using a polysulphone membrane.

Claim 10 (Previously Presented) The process according to claim 1, wherein the microfiltration process is performed as a batch process.

Claim 11 (Previously Presented) The process according to claim 1, wherein the microfiltration process is performed as a continuous process.

Claim 12 (Previously Presented) The process according to claim 1, wherein the microfiltration process is followed by an ultrafiltration process.

Claim 13 (Previously Presented) The process according to claim 12, wherein the cut-off value of the ultrafiltration membrane is lower than four times the molecular weight of the fermentation-derived product.

Claim 14 (Previously Presented) The process according to claim 12, wherein the cut-off value of the ultrafiltration membrane is lower than twice the molecular weight of the fermentation-derived product.

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Claim 15 (Previously Presented) The process according to claim 12, wherein the cut-off value of the ultrafiltration membrane is lower than the molecular weight of the fermentation-derived product.

Claim 16 (Previously Presented) The process according to claim 1, wherein the microfiltration process is followed by at least one chromatographic step or at least one precipitation step.

Claim 17 (Previously Presented) The process according to claim 1, wherein the product is at temperatures higher than 66 °C for less than 60 minutes.

Claim 18 (Previously Presented) The process according to claim 1, wherein the product is at temperatures higher than 66 °C for less than 30 minutes.

Claim 19 (Previously Presented) The process according to claim 1, wherein the product is at temperatures higher than 66 °C for less than 15 minutes.

Claim 20 (Previously Presented) The process according to claim 1, wherein the product is at temperatures higher than 66 °C for less than 10 minutes.

Claims 21-22 (Cancelled)

Claim 23 (Currently Amended) The process according to claim 22 1, wherein the host cell producing said protein is selected from the group consisting of *E. coli*, *Saccharomyces*, *Pichia*, *Candida* and *Kluyveromyces*.

Claims 24-25 (Cancelled)

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Claim 26 (Currently Amended) The process according to claim 24 1, wherein the product protein is a protein with a molar weight of less than 10000 Dalton.

Claim 27 (Currently Amended) The process according to claim 24 1, wherein the product protein is a protein with a molar weight of less than 7000 Dalton.

Claim 28 (Currently Amended) The process according to claim 24 1, wherein the product protein is a protein with a molar weight of less than 4000 Dalton.

Claim 29 (Currently Amended) The process according to claim 24 1, wherein said protein is selected from the group consisting of glucagon-like peptide 1 (GLP-1), glucagon-like peptide 2 (GLP-2), glucagon, trefoil factor (TFF) peptides, interleukins, insulin, albumin, precursors thereof and analogs of any of the foregoing.

Claim 30 (Previously Presented) The process according to claim 29, wherein said protein is selected from the group consisting of human insulin, a human insulin precursor, a human insulin analog, a human insulin analog precursor, and Arg³⁴-GLP-1(7-37).

Claim 31 (Previously Presented) The process according to claim 29, wherein said protein is selected from the group consisting of Arg³⁴-GLP-1(7-37), Gly⁸-GLP-1(7-36)-amide, Gly⁸-GLP-1(7-37), Val⁸-GLP-1(7-36)-amide, Val⁸-GLP-1(7-37), Val⁸Asp²²-GLP-1(7-36)-amide, Val⁸Asp²²-GLP-1(7-37), Val⁸Glu²²-GLP-1(7-36)-amide, Val⁸Glu²²-GLP-1(7-37), Val⁸Lys²²-GLP-1(7-36)-amide, Val⁸Lys²²-GLP-1(7-37), Val⁸Arg²²-GLP-1(7-36)-amide, Val⁸Arg²²-GLP-1(7-37), Val⁸His²²-GLP-1(7-36)-amide, Val⁸His²²-GLP-1(7-37), Val⁸Trp¹⁹Glu²²-GLP-1(7-37), Val⁸Glu²²Val²⁵-GLP-1(7-37), Val⁸Tyr¹⁶Glu²²-GLP-1(7-37), Val⁸Trp¹⁶Glu²²-GLP-1(7-37), Val⁸Leu¹⁶Glu²²-GLP-1(7-37), Val⁸Tyr¹⁸Glu²²-GLP-1(7-37), Val⁸Glu²²His³⁷-GLP-1(7-37), Val⁸Glu²²Ile³³-GLP-1(7-37), Val⁸Trp¹⁶Glu²²Val²⁵Ile³³-GLP-1(7-37),

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Val⁸Trp¹⁶Glu²²Ile³³-GLP-1(7-37), Val⁸Glu²²Val²⁵Ile³³-GLP-1(7-37), Val⁸Trp¹⁶Glu²²Val²⁵-GLP-1(7-37) and analogs thereof.

Claim 32 (Previously Presented) The process according to claim 29, wherein said protein is selected from the group consisting of: K30R-GLP-2(1-33); S5K-GLP-2(1-33); S7K-GLP-2(1-33); D8K-GLP-2(1-33); E9K-GLP-2(1-33); M10K-GLP-2(1-33); N11K-GLP-2(1-33); T12K-GLP-2(1-33); I13K-GLP-2(1-33); L14K-GLP-2(1-33); D15K-GLP-2(1-33); N16K-GLP-2(1-33); L17K-GLP-2(1-33); A18K-GLP-2(1-33); D21K-GLP-2(1-33); N24K-GLP-2(1-33); Q28K-GLP-2(1-33); S5K/K30R-GLP-2(1-33); S7K/K30R-GLP-2(1-33); D8K/K30R-GLP-2(1-33); E9K/K30R-GLP-2(1-33); M10K/K30R-GLP-2(1-33); N11K/K30R-GLP-2(1-33); T12K/K30R-GLP-2(1-33); I13K/K30R-GLP-2(1-33); L14K/K30R-GLP-2(1-33); D15K/K30R-GLP-2(1-33); N16K/K30R-GLP-2(1-33); L17K/K30R-GLP-2(1-33); A18K/K30R-GLP-2(1-33); D21K/K30R-GLP-2(1-33); N24K/K30R-GLP-2(1-33); Q28K/K30R-GLP-2(1-33); K30R/D33K-GLP-2(1-33); D3E/K30R/D33E-GLP-2(1-33); D3E/S5K/K30R/D33E-GLP-2(1-33); D3E/S7K/K30R/D33E-GLP-2(1-33); D3E/D8K/K30R/D33E-GLP-2(1-33); D3E/E9K/K30R/D33E-GLP-2(1-33); D3E/M10K/K30R/D33E-GLP-2(1-33); D3E/N11K/K30R/D33E-GLP-2(1-33); D3E/T12K/K30R/D33E-GLP-2(1-33); D3E/I13K/K30R/D33E-GLP-2(1-33); D3E/L14K/K30R/D33E-GLP-2(1-33); D3E/D15K/K30R/D33E-GLP-2(1-33); D3E/N16K/K30R/D33E-GLP-2(1-33); D3E/L17K/K30R/D33E-GLP-2(1-33); D3E/A18K/K30R/D33E-GLP-2(1-33); D3E/D21K/K30R/D33E-GLP-2(1-33); D3E/N24K/K30R/D33E-GLP-2(1-33); D3E/Q28K/K30R/D33E-GLP-2(1-33); and precursors thereof

Claim 33 (Currently Amended) The process according to claim 24-1, wherein said protein is exendin-3, exendin-4 or analogs thereof and precursors of any of the foregoing.

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Claim 34 (Previously Presented) The process according to claim 33, wherein said protein is ZP-10 (HGEGTFTSDL SKQMEEEA VRLFIEWLKN GGPSSG APPSK KKKKK-NH₂).

Claim 35 (New) A process for purifying a fermentation-derived protein, said process comprising microfiltration of a fermentation broth containing the protein at a microfiltration temperature within the range from 66 °C to 90 °C and wherein the host cell producing said protein is selected from the group consisting of *E. coli*, *Saccharomyces*, *Pichia*, *Candida* and *Kluyveromyces*.